510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY TEMPLATE

A. 510(k) Number:

k140089

B. Purpose for Submission:

New Device

C. Measurand:

Oxazepam, Morphine

D. Type of Test:

Qualitative lateral flow chromatographic immunoassay

E. Applicant:

Guangzhou Wondfo Biotech Co., Ltd.

F. Proprietary and Established Names:

CR3 Keyless Split Sample Cup Morphine-Oxazepam

G. Regulatory Information:

Product Code	Classification	Regulation Section	Panel
DJG	Class II	21 CFR 862.3650, Opiate Test System	Toxicology (91)
JXM	Class II	21 CFR 862.3170, Benzodiazepine Test System	Toxicology (91)

H. Intended Use:

1. Intended use(s):

   See Indication(s) for use.

2. Indication(s) for use:

   CR3 Keyless Split Sample Cup Morphine-Oxazepam is a rapid test for the qualitative detection of Morphine (a drug in the opiate class) and Oxazepam (a drug in the

benzodiazepine class) in human urine at a cutoff concentration of 2000 ng/mL and 300ng/mL, respectively.

The tests may yield preliminary positive results even when prescription drugs including Morphine and Oxazepam are ingested at prescribed doses; it is not intended to distinguish between prescription use or abuse of these drugs. There are no uniformly recognized cutoff concentration levels Morphine or Oxazepam in urine. The test provides only preliminary test results. A more specific alternative chemical method must be used in order to obtain a confirmed analytical result. GC/MS is the preferred confirmatory method. Clinical consideration and professional judgment should be exercised with any drug of abuse test result, particularly when the preliminary result is positive.

For in vitro diagnostic use only. It is intended for over-the-counter and for prescription use.

3. Special conditions for use statement(s):

   For Over the Counter and Prescription Use

   For *in vitro* diagnostic use only

4. Special instrument requirements:

   Not applicable. Device is visually read, single use device.

I. Device Description:

Each pouch contains a test cup and test card test card.

The OTC device also includes labeled vials for shipping the "preliminary" sample to the laboratory for confirmation, plastic transportation bags, mailing boxes, and personal identification numbers

Each test strip in the device consists of a conjugate pad containing colloidal gold coupled with the anti-drug antibodies and a nitrocellulose membrane containing two test lines coated with the conjugated drug antigen, and a procedural control line.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   Wondfo Multi-Drug Urine Test Cup (Panel)

2. Predicate 510(k) number(s):

   k130665

3. Comparison with predicate:

Item	Device	Predicate (K130665)
Indication(s) for use	For the qualitative determination of Morphine and Oxazepam in human urine.	Same
Methodology	Competitive binding, lateral flow immunochromatographic assays based on the principle of antigen antibody immunochemistry.	Same
Results	Qualitative	Same
Specimen Type	Human urine	Same
Cut Off Values	Morphine: 2000ng/ml Oxazepam: 300ng/ml	Same
Configurations	Split Keyless CupSplit Sample	Cup, Dip Card
Intended Use	OTC Use & Prescription Use	Same

K. Standard/Guidance Document Referenced (if applicable):

Not Applicable

L. Test Principle:

The device is a rapid test for the qualitative detection of Morphine and Oxazepam in urine samples. It is a lateral flow chromatographic immunoassay. When the absorbent end is immersed into a urine sample, the urine is absorbed into the device by capillary action and mixes with the antibody-dye conjugate, flowing across the pre-coated membrane. At analyte concentrations below the target cutoff, antibody-dye conjugates bind to the drug-protein conjugate immobilized in the Test Region (T) of the device. This produces a colored test line that indicates a negative result. When the analyte concentration is above the cutoff, analyte molecules bind to the antibody-dye conjugate, preventing the antibody-dye conjugate from binding to the drug-protein conjugate immobilized in the Test Region (T) of the device. When the sample contains target drug above the cutoff concentration no colored band shows in the test region, indicating a preliminary positive result.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Precision studies were carried out for urine samples with concentrations of -100%cutoff, -75%cutoff, -50%cutoff, -25%cutoff, +25%cutoff, +50%cutoff , +75%cutoff and +100%cutoff. For each concentration, tests using masked and randomized samples were performed by three operators twice per day for 25 days with three different lots of devices. The results obtained are summarized in the following tables.

Morphine Testing

Results per Lot	-100% cut off	-75% cut off	-50% cut off	-25% cut off	cut off 2000 ng/mL	+25% cut off	+50% cut off	+75% cut off	+100% cut off
Lot 1	50-/0+	50-/0+	50-/0+	50-/0+	43+/7-	50+/0-	50+/0-	50+/0-	50+/0-
Lot 2	50-/0+	50-/0+	50-/0+	50-/0+	44+/6-	50+/0-	50+/0-	50+/0-	50+/0-
Lot 3	50-/0+	50-/0+	50-/0+	50-/0+	43+/7-	50+/0-	50+/0-	50+/0-	50+/0-

Oxazepam Testing

Results per Lot	-100% cut off	-75% cut off	-50% cut off	-25% cut off	cut off 300 ng/mL	+25% cut off	+50% cut off	+75% cut off	+100% cut off
Lot 1	50-/0+	50-/0+	50-/0+	50-/0+	43+/7-	50+/0-	50+/0-	50+/0-	50+/0-
Lot 2	50-/0+	50-/0+	50-/0+	50-/0+	44+/6-	50+/0-	50+/0-	50+/0-	50+/0-
Lot 3	50-/0+	50-/0+	50-/0+	50-/0+	43+/7-	50+/0-	50+/0-	50+/0-	50+/0-

b. Linearity/assay reportable range:

Not applicable

c. Traceability, Stability, Expected values (controls, calibrators, or methods):

Quality control materials are not supplied with these devices. The labeling contains recommendations to confirm the test procedure and to verify proper test performance, the sponsor recommends that the user test these devices using external controls following the appropriate federal, state and local guidelines.

Accelerated stability and real time stability tests were performed on three lots of dip cards and cups for morphine and oxazepam urine test devices using samples at -50% cutoff and +50% cutoff, and negative urine. The stability study results support the claimed shelf life of 18 months at 4 to 30 ºC. The transport simulation study results support stability for 3 weeks when exposed to temperatures of ranging from -20 ºC and 40 ºC.

d. Detection limit:

Not applicable. The assay is intended for qualitative use.

e. Analytical specificity:

Analytical specificity studies were performed to determine whether drugs and drug metabolites within the same class of drugs or with similar molecular structures cross- react in the test system.

The target drug, drug metabolites, and other related compounds were added to drug-free urine. The cross reacting substances and the lowest concentration that produces a positive result was identified. A list of these compounds and their level of cross reactivity is provided in the tables below:

Morphine, Cutoff=2000 ng/mL	**Result** Positive at 2,000 ng/mL	**%Cross-Reactivity**
Codeine	Positive at 2,000 ng/mL	100%
Ethylmorphine	Positive at 5,000 ng/mL	40%
Hydrocodone	Positive at 12,500 ng/mL	16%
Hydromorphone	Positive at 5,000 ng/mL	40%
Levorphanol	Positive at 75,000 ng/mL	2.7%
σ-Monoacetylmorphine	Positive at 5,000 ng/mL	40%
Morphine 3-b-D-glucuronide	Positive at 2,000 ng/mL	100%
Norcodeine	Positive at 12,500 ng/mL	16%
Normorphone	Positive at 50,000 ng/mL	4%
Oxycodone	Positive at 25,000 ng/mL	8%
Oxymorphone	Positive at 25,000 ng/mL	8%
Procaine	Positive at 150,000 ng/mL	1.3%
Thebaine	Positive at 100,000 ng/mL	2%

Oxazepam, Cutoff=300 ng/mL	**Result** Positive at 300 ng/mL	**%Cross-Reactivity**
Alprazolam	Positive at 200 ng/mL	150%
α-Hydroxyalprazolam	Positive at 1,500 ng/mL	20%

Bromazepam	Positive at 1,500 ng/mL	20%
Chlordiazepoxide	Positive at 1,500 ng/mL	20%
Clonazepam HCl	Positive at 800 ng/mL	37.5%
Clobazam	Positive at 100 ng/mL	300%
Clonazepam	Positive at 800 ng/mL	37.5%
Clorazepate dipotassium	Positive at 200 ng/mL	150%
Delorazepam	Positive at 1,500 ng/mL	20%
Desalkylflurazepam	Positive at 400 ng/mL	75%
Diazepam	Positive at 200 ng/mL	150%
Estazolam	Positive at 2,500 ng/mL	12%
Flunitrazepam	Positive at 400 ng/mL	75%
D,L-Lorazepam	Positive at 1,500 ng/mL	20%
Midazolam	Positive at 12,500 ng/mL	2.4%
Nitrazepam	Positive at 100 ng/mL	300%
Norchlordiazepoxide	Positive at 200 ng/mL	150%
Nordiazepam	Positive at 400 ng/mL	75%
Temazepam	Positive at 100 ng/mL	300%
Trazolam	Positive at 2,500 ng/mL	12%

Interference Studies:

Interference studies were performed using 100 µg/mL of structurally unrelated compounds as well as endogenous compounds listed below.. These compounds were tested in drug-free urine and urine containing ±25% cutoff concentration for each analyte. The following compounds were found not to interfere when tested at 100 µg/mL concentration.

Morphine

4-Acetamidophenol	Ecgonine methylester	Oxolinic acid
Acetophenetidin	(-) -Y -Ephedrine	Oxymetazoline
N-Acetylprocainamide	Erythromycin	Papaverine
Acetylsalicylic acid	β-Estradiol	Penicillin-G
Aminopyrine	Estrone-3-sulfate	Pentazocine
Amitryptyline	Ethyl-p-aminobenzoate	Pentobarbital
Amobarbital	Fenoprofen	Perphenazine
Amoxicillin	Furosemide	Phencyclidine
Ampicillin	Gentisic acid	Phenelzine
Ascorbic acid	Hemoglobin	Phenobarbital
D,L-Amphetamine	Hydralazine	Phentermine
Apomorphine	Hydrochlorothiazide	L-Phenylephrine
Aspartame	Hydrocortisone	β-Phenylethylamine

Atropine	O-Hydroxyhippuric acid	Phenylpropanolamine
Benzilic acid	p-Hydroxy methamphetamine	Prednisone
Benzoic acid	3-Hydroxytyramine	D,L-Propanolol
Benzoylecgonine	Ibuprofen	D-Propoxyphene
Benzphetamine	Imipramine	D-Pseudoephedrine
Bilirubin (±)	Iproniazid	Quinidine
Brompheniramine	Isoproterenol	Quinine
Caffeine	Isoxsuprine	Ranitidine
Cannabidiol	Ketamine	Salicylic acid
Chloral hydrate	Ketoprofen	Secobarbital
Chloramphenicol	Labetalol	Serotonin (5-Hydroxytyramine)
Chlordiazepoxide	Loperamide	Sulfamethazine
Chlorothiazide	Maprotiline	Sulindac
(±) Chlorpheniramine	Meperidine	Temazepam
Chlorpromazine	Meprobamate	Tetracycline
Chlorquine	Methadone	Tetrahydrocortisone, 3 Acetate
Cholesterol	Methoxyphenamine	Tetrahydrocortisone3 (β-D glucuronide)
Clomipramine	(+) 3,4-Methylenedioxy-amphetamine	Tetrahydrozoline
Clonidine	(+)3,4-Methylenedioxy-methamphetamine	Thiamine
Cocaine hydrochloride	Nalidixic acid	Thioridazine
Cortisone	Nalorphine	D, L-Tyrosine
(-) Cotinine	Naloxone	Tolbutamide
Creatinine	Naltrexone	Triamterene
Deoxycorticosterone	Naproxen	Trifluoperazine
Dextromethorphan	Niacinamide	Trimethoprim
Diazepam	Nifedipine	Trimipramine
Diclofenac	Norethindrone	Tryptamine
Diflunisal	D-Norpropoxyphene	D, L-Tryptophan
Digoxin	Noscapine	Tyramine
Diphenhydramine	D,L-Octopamine	Uric acid
Doxylamine	Oxalic acid	Verapamil
Ecgonine hydrochloride	Oxazepam	Zomepirac

Oxazepam

4-Acetamidophenol	Doxylamine	Oxolinic acid
Acetophenetidin	Ecgonine hydrochloride	Pentobarbital
N-Acetylprocainamide	Ecgonine methylester	Perphenazine
Acetysalicylic acid	(-)-Y-Ephedrine	Phencyclidine
Aminopyrine	Fenoprofen	Phenelzine
Amitriptyline	Furosemide	Phenobarbital
Amorbarbital	Gentisic acid	Phentermine
Amoxicillin	Hemoglobin	L-Phenylephrine
Ampicillin	Hydrocortisone	-Phenylethylamine
l-Ascorbic Acid	O-Hydroxyhippuric acid	Phenylpropanolamine
D.L-Amphetamine	p-Hydroxy-methamphetamine	Prednisone
Apomorphine	3-Hydroxytyramine	D.L-Propranolol
Aspartame	Ibuprofen	D-Propoxyphene
Atropine	Imipramine	D-Pseudoephedrine
Benzilic acid	Iproniazid	Quinine
Benzoic acid	(±)Isoproterenol	Ranitidine
Benzoylecgonine	Isoxsuprine	Salicylic acid
Benzphetamine	Ketamine	Secobarbital
Bilirubin	Ketoprofen	Serotonin (5-Hydroxytyramine)
(±) Chlorpheniramine	Labetalol	Sertraline
Caffeine	Loperamide	Sulfamethazine
Cannabidiol	Maprotiline	Sulindac
Chloral hydrate	Meperidine	Tetrahydrocortisone, 3 Acetate
Chloramphenicol	Meprobamate	Tetrahydrocortisone,(-D glucuronide)
Chlorothiazide	Methadone	Tetrahydrozoline
(±)Chlorpheniramine	Methoxyphenamine	Thiamine
Chlorpromazine	(+) 3,4-Methylenedioxy-amphetamine	Thioridazine
Chloroquine	(+)3,4-Methylenedioxy-methamphetamine	D.L-Tyrosine
Cholesterol	Nalidixic acid	Tolbutamide
Clomipramine	Nalorphine	Triamterene
Clonidine	Naloxone	Trifluoperazine
Cocaine hydrochloride	Naltrexone	Trimethoprim

Cortisone	Naproxen	Tryptamine
(-)cotinine	Niacinamide	D.L-Tryptophan
Creatinine	Nifedipine	Tyramine
Dextromethorphan	Norethindrone	Uric acid
Diclolfenac	D-Norpropoxyphene	Verapamil
Diflunisal	Noscapine	Zomepirac
Dioxin	D.L-Octopamine	
Diphenhydramine	Oxalic acid	

Specific Gravity:

Twelve urine samples with density ranges (1.000-1.035) were collected and spiked with each drug at 25% below and 25% above cutoff levels. Each sample was tested using three lots of CR3 Keyless Split Sample Cup Morphine-Oxazepam. The results showed that specific gravity range of 1.000 to 1.035 does not affect the accuracy of the test.

pH:

A negative urine pool was adjusted to a pH range of 4.00 to 9.00 in 1 pH unit increments and was spiked with each drug at 25% below and 25% above cutoff levels. Samples were tested using three lots of CR3 Keyless Split Sample Cup Morphine-Oxazepam and results showed that urine pH range of 4.00 to 9.00 does not affect the accuracy of the accuracy of the test.

f. Assay cut-off:

Characterization of how the device performs around the claimed cutoff concentration is shown in the precision section M.1.a. above as well as the Lay User Study below.

2. Comparison studies:

a. Method comparison with predicate device:

The method comparison for the CR3 Keyless Split Sample Cup Morphine-Oxazepam was performed at the manufacturer's site.. Operators ran 80 unaltered masked and randomized clinical samples. The samples were compared to GC/MS results. Four "viewers" separately read results (3 experienced viewers, 1 OTC viewer). Viewers A, B, and C in the table below were experienced professionals. Viewer D was a lay person. The results are presented in the table below:

Morphine

Results per Operator		Negative	Low Negative by GC/MS (less than -50%)	Near Cutoff Negative by GC/MS (Between -50% and	Near Cutoff Positive by GC/MS (Between the cutoff and +50%)	High Positive by GC/MS (greater than +50%)
Viewer A	Positive	0	0	2	19	20
	Negative	10	20	8	1	0
Viewer B	Positive	0	0	3	18	20
	Negative	10	20	7	2	0
Viewer C	Positive	0	0	2	18	20
	Negative	10	20	8	2	0
Viewer D	Positive	0	0	3	18	20
	Negative	10	20	7	2	0

The following table lists the CR3 Keyless Split Sample results and GCMS results for the discordant samples shown in the table above.

GC/MS Morphine Concentration (ng/mL)	CR3 Morphine Result
1997	Positive
1994	Positive
2025	Negative
1994	Positive
2025	Negative
1943	Positive (for viewers B and D)
2043	Negative (for viewers (B, C, and D)

Oxazepam

Results per Operator		Negative	Low Negative by GC/MS (less than -50%)	Near Cutoff Negative by GC/MS (Between -50% and	Near Cutoff Positive by GC/MS (Between the cutoff and +50%)	High Positive by GC/MS (greater than +50%)
Viewer A	Positive	0	0	2	17	21
	Negative	10	10	18	2	0
Viewer B	Positive	0	0	3	18	21
	Negative	10	10	17	1	0
Viewer C	Positive	0	0	2	16	21
	Negative	10	10	18	3	0
Viewer D	Positive	0	0	3	15	21
	Negative	10	10	17	4	0

The following table lists the CR3 Keyless Split Sample results and GCMS results for the discordant samples shown in the table above.

GC/MS Oxazepam Concentration (ng/mL)	CR3 results
357	Negative
296	Positive
358	Negative for viewers A, C, D
344	Negative for viewers A, C, D
312	Negative for viewers B, C, D
288	Positive for 3 viewers B, C, D
291	Positive for viewers A, B, D

A lay user study was performed at three sites with 260 lay persons. In the study, 79 males and 47 females tested the Morphine samples and 74 males and 60 females tested the Oxazepam samples. The participants had diverse educational and professional backgrounds and ranged in age from 21 to >50. Urine samples were prepared at the following concentrations; -100%, +/-75%, +/-50%, +/-25% of the cutoff by spiking drug(s) into drug free-pooled urine specimens. The concentrations of the samples were confirmed by GC/MS. Each sample was aliquoted into

individual containers. Each participant was provided with the package insert, one masked and randomized sample, and a device. The results are summarized below.

Drug	Concentration	Number of samples	Negative	Positive	%Agreement With GC/MS
Drug -free	-100%	20	20	0	100%
Morphine	-75%	20	20	0	100%
	-50%	20	20	0	100%
	-25%	20	18	2	90%
	+25%	20	3	17	85%
	+50%	20	0	20	100%
	+75%	20	0	20	100%
Oxazepam	-75%	20	20	0	100%
	-50%	20	20	0	100%
	-25%	20	17	3	85%
	+25%	20	3	17	85%
	+50%	20	0	20	100%
	+75%	20	0	20	100%

b. Matrix comparison:

Not applicable. The assay is intended for use with urine samples only.

3. Clinical studies:

a. Clinical Sensitivity:

Not applicable

b. Clinical specificity:

Not applicable

c. Other clinical supportive data (when a. and b. are not applicable):

Not applicable

4. Clinical cut-off:

Not applicable

5. Expected values/Reference range:

   Not applicable

N. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

O. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.